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Small Supratentorial, Extraaxial Primitive Neuroectodermal Tumor Causing Large Intracerebral Hematoma

-Case Report-

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Abstract

A 16-year-old boy presented with an unusual case of a supratentorial, extraaxial small round blue cell tumor of the central nervous system, which was most likely a primitive neuroectodermal tumor (PNET). Preoperative computed tomography and magnetic resonance imaging showed a large multistage hematoma in the left central region. Intraoperatively, a small, superficial tumorous lesion was found between the sagittal sinus and a large cortical vein hidden by the hematoma. The histological diagnosis was PNET. This tumor is one of the most aggressive intracerebral tumors, not only in children, so treatment strategies must be early, profound, and interdisciplinary. This case represents an important example of atypical extraaxial appearance of this lesion, which should be considered in the differential diagnosis of cortical or subcortical hemorrhage, since complete resection of this lesion is critical for the successful treatment and outcome.

Introduction

Supratentorial primitive neuroectodermal tumors (PNETs) belong to a heterogeneous group of undifferentiated or poorly differentiated tumors called small round blue cell tumors (SRBCTs)[9,16] of the central nervous system (CNS), which occur predominantly in children or young adults.[8,12] Recently, supratentorial PNETs were grouped together with all extracerebellar PNETs and renamed CNS PNET.[11] Supratentorial PNETs are less common than cerebellar PNETs and account for 2-3% of all childhood brain tumors with a peak in the first 3 years of life.[18] Preoperative neuroradiological findings vary and may consist of an enhanced lesion on T1- and T2-weighted magnetic resonance (MR) imaging or computed tomography (CT) with contrast medium, associated with cystic and necrotic portions, perifocal edema, or hemorrhage.[4] Initiation of early and interdisciplinary adjuvant treatment for PNETs after complete neurosurgical resection is critical for the patient, since these tumors show much more aggressive behavior and the treatment options are poorly defined compared to infratentorial counterparts.

We describe a case of SRBCT obscured by a large intracerebral hemorrhage on preoperative imaging and hardly visible intraoperatively, which complicated the establishment of the diagnosis.

Case Report

A 16-year-old boy with previously unremarkable medical history was referred from a community hospital to our department with a progressive sensorimotor brachiofacial hemisyndrome on the right. His symptoms had developed mildly over 2 weeks, but he developed nearly complete paralysis of the right arm while playing in a field hockey game on the day of admission.

CT and MR imaging showed a large (5.2 x 4.8 x 4.7 cm) hemorrhage in the left central area with signs of multistage bleeding with little perifocal edema (Fig. 1). No tumor was visible. CT angiography, MR angiography, and conventional angiography revealed no signs of vascular lesions, in particular no arteriovenous or venous malformations.

Emergency neurosurgical resection was performed within the first hours of admission due to his decreasing level of consciousness. During surgery the patient was placed in the supine position and his head was fixed with a Mayfield head holder. The hematoma was localized using neuro-navigation and a craniotomy was performed. After dura opening, the superficial part of the hematoma was visible at the level of the cortical surface, and the hematoma could be quickly removed by suctioning. On closer inspection, we discovered a small (approx. 3 x 3 mm), high cortical, superficial lesion, seemingly located in a subarachnoid plane between the sagittal sinus and a large cortical vein (Fig. 2). The lesion was soft, highly vascularized, and bright red. The lesion was removed gross totally. The rest of the hematoma cavity showed no macroscopic abnormalities.

Histological examination revealed a heterogeneous, pleomorphic tumor with unclear borders and a high proliferation index (Ki-67) of over 30% with atypic mitotic and apoptotic pattern (Fig. 3A, B, D). The resected lesion revealed the criteria for SRBCT and the diagnosis was verified by a second opinion from the Cancer Reference Center in Bonn and Kiel, Germany. Immunohistochemical investigations excluded neuronal or glial components (negative for glial fibrillary acidic protein, neurofilament protein, and synaptophysin) or embryonic tumors with atypical teratogenic/rhabdoid

fractions by molecular analyses (negative for t11/22, and no nuclear INI-1 lost). CD99 staining for peripheral PNET was positive with a membranous pattern (Fig. 3C).

The postoperative course was uneventful and the hemiparesis of the right arm improved significantly during the first postoperative week. Postoperative CT and MR imaging showed complete removal of the hematoma and no signs of tumor remnant (Fig. 4). The postoperative staging revealed negative lumbar puncture and biopsies of bone marrow and muscle were negative for malignant cells. Axial MR imaging of the spine showed a small (0.2 x 0.2 cm) single intraspinal enhanced lesion (T11) suggestive of leptomeningeal dissemination, which could not be confirmed by positron emission tomography imaging and follow-up MR imaging 3 months later. After sperm cryopreservation, adjuvant radiation with boost to the whole neuraxis and brain was initiated 4 weeks after surgery for 6 weeks followed by chemotherapy with cisplatin.

Discussion

SRBCT including CNS or peripheral PNETs are high-grade malignant cerebral tumors, which affect both the pediatric and adult population.[12)] Treatment is often challenging and frustrating due to the poor prognosis, and depends on many risk factors such as localization of the lesion and grade of staging at diagnosis.[3,5)] Compared to other embryonic malignant tumors such as medulloblastoma with better established treatment regimes, the optimum treatment of this rare and heterogeneous tumor group is still the subject of research and many clinical studies are ongoing.[10,14,19,22)] Today, surgery is recommended for the care of PNET patients (>3 years of age) followed by radiation[14)] and chemotherapy.[8,20)] No standards have been established, high dose chemotherapy with different regimes may be better before radiation in younger children.[7,13)] In contrast,

radiation directly after surgery is recommended before chemotherapy in older children or adults.[17)]

On this account, cases of SRBCT need to be analyzed in great detail in order to gain data for future treatment options. Until then, it is critical to guarantee the best starting position for radiation and chemotherapy by surgical resection, and therefore identification of this lesion as soon as possible is important. Due to the heterogeneity of this embryonic tumor group, neuroradiological findings are usually non-uniform and may hinder or delay the diagnosis.[4)] For example, analysis of 13 pediatric patients with CNS PNETs found heterogeneous neuroradiological findings whereas only 3 cases revealed radiological signs of hemorrhage.[6)] In contrast to the uncommon appearance of hemorrhagic areas, cystic parts and foci of calcification were more frequently found as described previously.[1)] However, in the present case, the lesion was surrounded by extensive intracerebral bleeding, and the clear and distinctive criteria for these tumors, such as cystic, necrotic, or contrast-enhanced parts,[4)] could not be detected on CT or MR imaging. The macroscopic view during surgery showed a small highly vascularized tumor, which could be completely resected. Although the precise pathophysiological mechanisms of hemorrhage into brain tumors are still under investigation, primitive tumors carry higher risk of bleeding than other types.[21)] The cause might be found in the dysmorphic configuration of the tumor vessels with endothelial abnormalities such as alteration of tight junctions, which render these lesions more hemorrhage-prone.[15)]

In this case, histological examination revealed the most likely criteria for peripheral PNET, based on the absence of staining against neuroepithelial antigens, and positive staining for CD99 in the membrane. Ewing family of tumors, especially the subgroup peripheral PNET and Ewing's sarcoma, usually highly express the *MIC*2 gene

product (CD99) and show chromosomal translocations such as t(11, 22)(q29; q12).[2)] In contrast, CNS PNETs are reported to be negative for both these features. In our case, the histological findings and extraaxial localization of the lesion strongly suggested that this SRBCT was a peripheral PNET rather than a CNS PNET, although no chromosomal translocations were detected in this tumor.

The present case shows that a small supratentorial, extraaxial PNET can be the cause of extensive acute intracerebral hemorrhage, although the tumor may not be detectable on preoperative MR imaging or CT. The present tumor was hidden in a small superficial, submeningeal pocket next to a cortical vein, so meticulous search for a tumorous lesion during hemorrhage evacuation is important, especially in the pediatric age group. Most aggressive tumor removal as soon as possible is critical to ensure the best start for radiation and chemotherapy in patients with SRBCT. The differential diagnosis of PNET should be considered in this heterogeneous tumor group with non-uniform neuroradiological findings, in particular with pediatric patients.

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Figure Legend

Fig. 1 A–C: Preoperative computed tomography scans with axial (A), coronal (B), and sagittal (C) reconstruction indicating the multistage hemorrhage. D–I: Axial T1-weighted (D), T1-weighted with contrast medium (E), and T2-weighted (F), as well as sagittal (G) and coronal (H) reconstructed T1-weighted with contrast medium and coronal T2-weighted (I) magnetic resonance images showing the hemorrhage located next to the sagittal sinus and a cortical vein. *Arrow* indicates approximately the area of the tumor which was found intraoperatively.

Fig. 2 Intraoperative microscope photograph showing a cortical vein (1), the tumorous lesion (2), and parts of the hematoma (3), with the suction (4) and bipolar devices (5).

Fig. 3 A, B: Photomicrographs of the removed tumorous tissue revealing a hemorrhagic pleomorphic (A, *arrows*) tumor with atypic mitotic (B, *arrows*) and apoptotic pattern. Hematoxylin and eosin stain, original magnification x100?. C, D: CD99 staining showing membranous immunopositivity (C), and MIB-1 (Ki-67) index of over 30% (D). *Arrows* indicate positive cells. Original magnification x100?.

Fig. 4 Postoperative computed tomography scans (A–C) and T1-weighted magnetic resonance images with contrast medium (D–F) with axial (A, D), coronal (B, E), and sagittal (C, F) reconstruction showing complete removal of the hematoma and no signs of tumor remnant.

Figure 1:

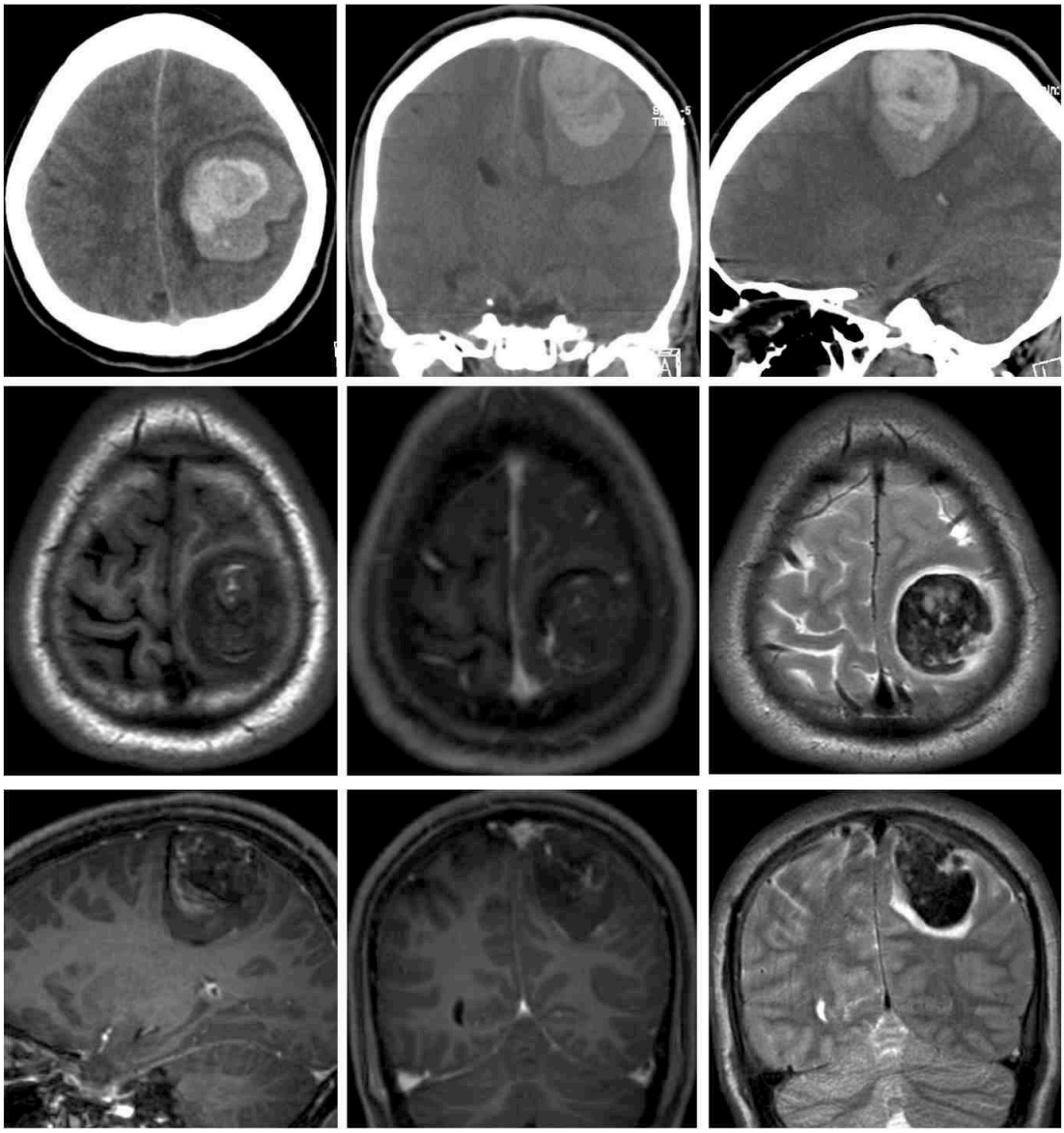

Figure 2:

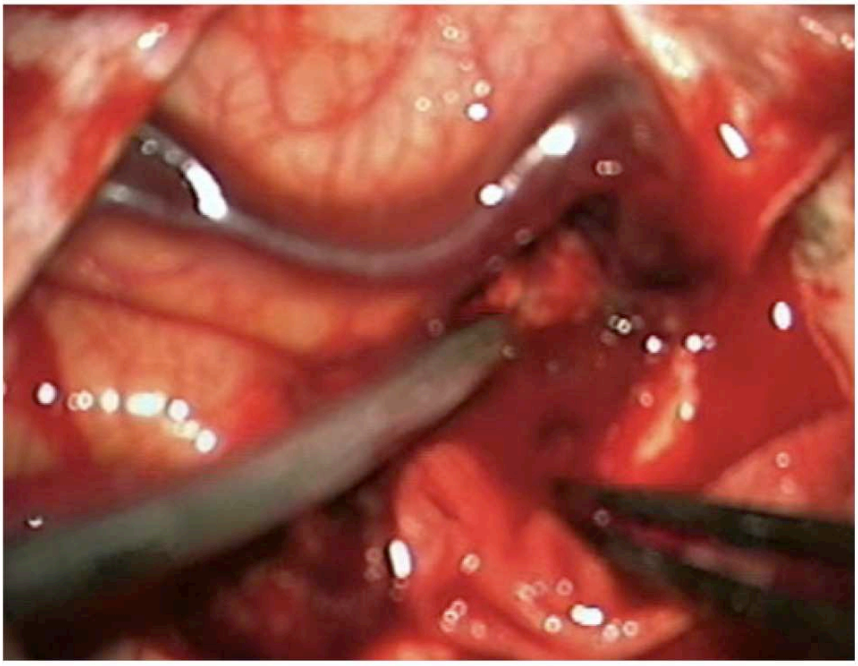

Figure 3:

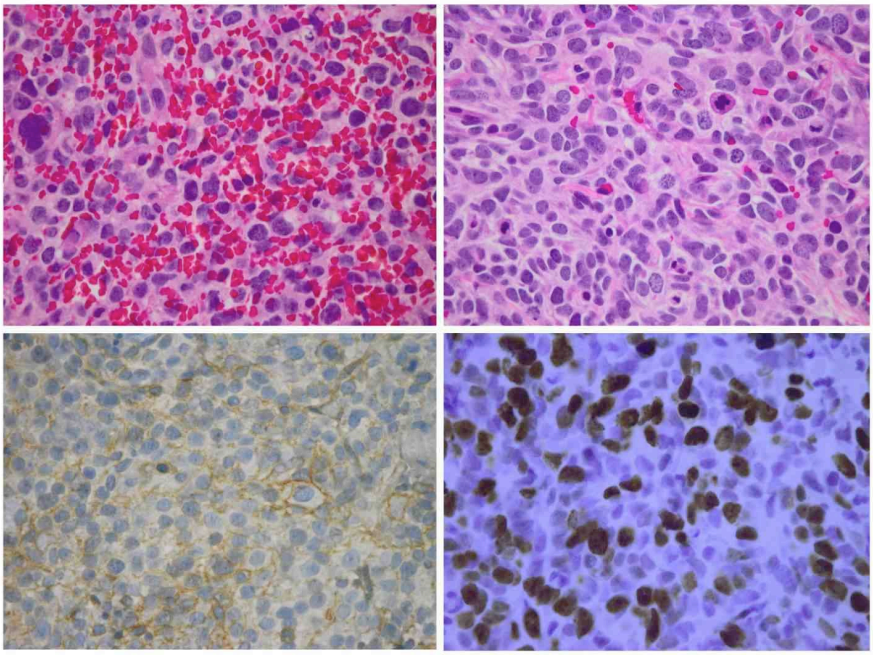

Figure 4: